

REMARKS

Claims 1-22 were pending in the present application. Upon entry of this response, claims 1, 7, and 12-14 have been amended. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Support for the amended claims can be found throughout the specification and claims as originally filed, and, in particular, on page 5, and at page 12, line 15. No new matter is believed to have been added.

Regarding the Information Disclosure Statement

The Applicants thank the Examiner his review of the cited references and for return of the initialed PTO-1449.

Regarding the Abstract

On pages 7-8 of the present Office Action, the Examiner reproduces the guidelines for the "proper language and format" for an abstract. Upon review of the abstracted submitted by the Applicants in the October 10, 2003 response to Office Action, the abstract as submitted appears to conform to the recited length and stylistic guidelines. The Applicants are therefore uncertain as to why the Examiner has reproduced the guidelines, and cannot find any specific comment addressed to the Applicants concerning the submitted abstract.

Should there be an informality or objection which the Applicants need to address, the undersigned would appreciate a telephone call or other communication from the Examiner detailing the correction needed.

Rejections under 35 U.S.C §103(a)

Claims 1-22 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO 97/47645 taken with Boeck et al., Jamison et al., and Balkovec et al. The Applicants respectfully traverse this rejection.

The Applicants assert that the limitations of claims 1-22, as amended, are not taught nor suggested by the references cited by the Examiner. In particular, WO 97/47645 does not teach nor suggest the structural features which are responsible for the increased water-solubility of the claimed adducts. As amended, claims 1, 7, and 12-14, and therefore their dependent claims, require that the adduct be more water soluble than the cyclic peptide prior to adduct formation. The Applicants, in order to expedite prosecution, have amended the claims to more particularly point out this feature of the claimed adducts and methods, and, as amended, the claims recite that the adduct be “ionic in character and has a tetrahedral geometry at the boron atom.” As explained on page 5 of the present application, the ionic, tetrahedral structure of the adducts enhances the hydrophilicity or water-solubility of the complexed material. Hence, materials containing a 1,2-*cis*-diol moiety that are generally insoluble or only slightly soluble in aqueous solutions can be made soluble or more soluble in aqueous solutions by forming the claimed borate or boronate adduct.

As stated in the response filed with the Office on October 20, 2003, the adducts as claimed differ from the phenylboronate complexes of formulae (III) and (IIIa) of WO 97/47645. These reference complexes are non-ionic borate esters and have a trigonal structure. The species obtained are both mono and diboron species, unlike the specific monoboron adducts taught in the present specification. As a result of the non-ionic, trigonal structure, the adducts of the reference are *less* water-soluble than the starting cyclopeptides. In contrast, the ionic, tetrahedral adducts claimed are *more* water-soluble than the starting cyclopeptides.

It is noted that, as stated in the specification, phenylboronic acid is a suitable boronic acid for producing the adducts as claimed, and it is incorrect to assume that phenylboronic acid always results in a trigonal planar adduct having reduced water-solubility, as obtained in the

reference. Depending on reaction conditions, it is possible to produce *either* the non-ionic, trigonal adduct, or the ionic, tetrahedral adduct as claimed. Further, the reference teaches the need to remove water and employs molecular sieves to do so, which teaches away from the conditions claimed in the present application. Additionally, the deprotection scheme of the reference utilizes 2N HCL to hydrolyze the boronate esters. Such a solution would have pH less than one, which is outside the pH ranged recited in the claims.

One of skill in the art, in view of the teachings of the present application would readily be able to produce the ionic tetrahedral adducts as claimed (see *e.g.*, page 5, line 7 through page 6, line 25; page 11, lines 6-24; and Example 1), while the specification of WO 97/47645, alone or in combination, does not teach or suggest formation of the adducts.

In view of the above remarks, the Applicants assert that WO 97/47645 does not disclose or suggest the limitations of the claims, as amended, as described by the Examiner. Indeed, as discussed above, the reference does not teach or suggest, either explicitly or implicitly the limitations of claims 1-3 or 7-10, and neither does a pH of “greater than 5” *necessarily* teach or suggest a pH value of “between 7.5 and 9.5”, as recited in claim 11.

Regarding the Examiner’s comments pertaining to Boeck et al., Jamison et al., and Balkovec et al. , the Applicants assert that these references alone, or in combination with WO 97/47645 do not teach nor suggest the limitations of claims 1-22, as amended. There is no teaching or suggestion in any of the references that *ionic, tetrahedral* adducts must be formed to enhance water solubility. Further, as noted in the October 20, 2003 response filed with the Office, Jamison et al. does **not** teach the use of boric or boronic acids and additionally, the hemiaminal described by Jamison et al. involves ether formation at only 1hydroxy of the 1,2-*cis*-diol, while the adducts of the present invention are complexed across both hydroxy groups. The Applicants do not see how the Jamison et al. hemiaminal can be considered analogous or suggestive to the present claims, alone or in combination with the other references.

As to Balkovec et al. specifically, the Applicants note that the passages referred to by the Examiner do not teach nor suggest the use of *boronic* or *boric* acids, which have been shown in the instant application to achieve unexpected and superior results, but rather teach the use of suitable acids, including “strong organic and mineral acids”. Examples given include methanesulfonic acid, hydrochloric acid and *hydrobromic* acid (Col. 7, lines 18-23). The Applicants do not understand how the purification of Balkovec can thus be characterized by the Examiner as “substantially the same method steps as claimed in claims 12 and 13...”

Turning to Broeck et al., the Applicants note that the disclosure on page 387 of the reference neither teaches nor suggests the limitations pertaining to the adduct as recited in the pending claims, and neither does the reference suggest the reversible nature of the adduct formation upon acidification, as recited in both the adduct and method claims. The echinocandins used in the Broeck et al., article were part of a fermentation broth, and there is no disclosure as to how to effect purification or product recovery while using boroic acid.

In view of the above remarks and amendments, the Applicants respectfully request withdrawal of the claim rejections under 35 U.S.C. §103(a).

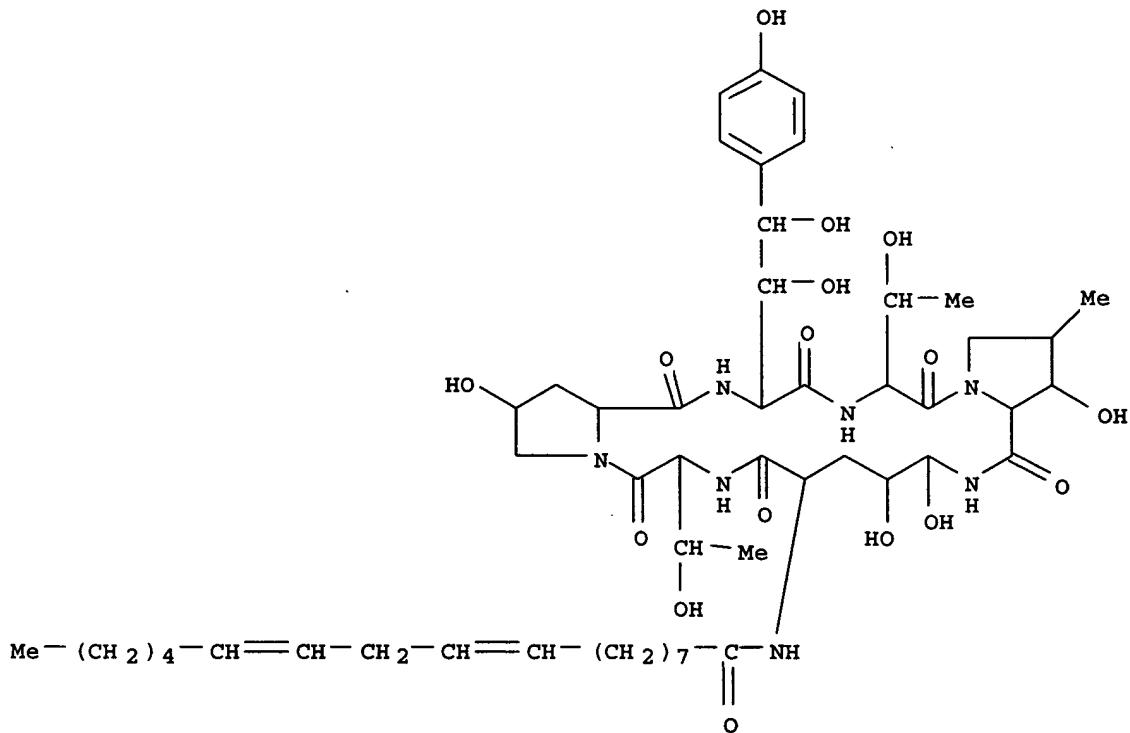
Rejections under 35 U.S.C 112

Claims 4-6, 8 and 18-22 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicants traverse this rejection.

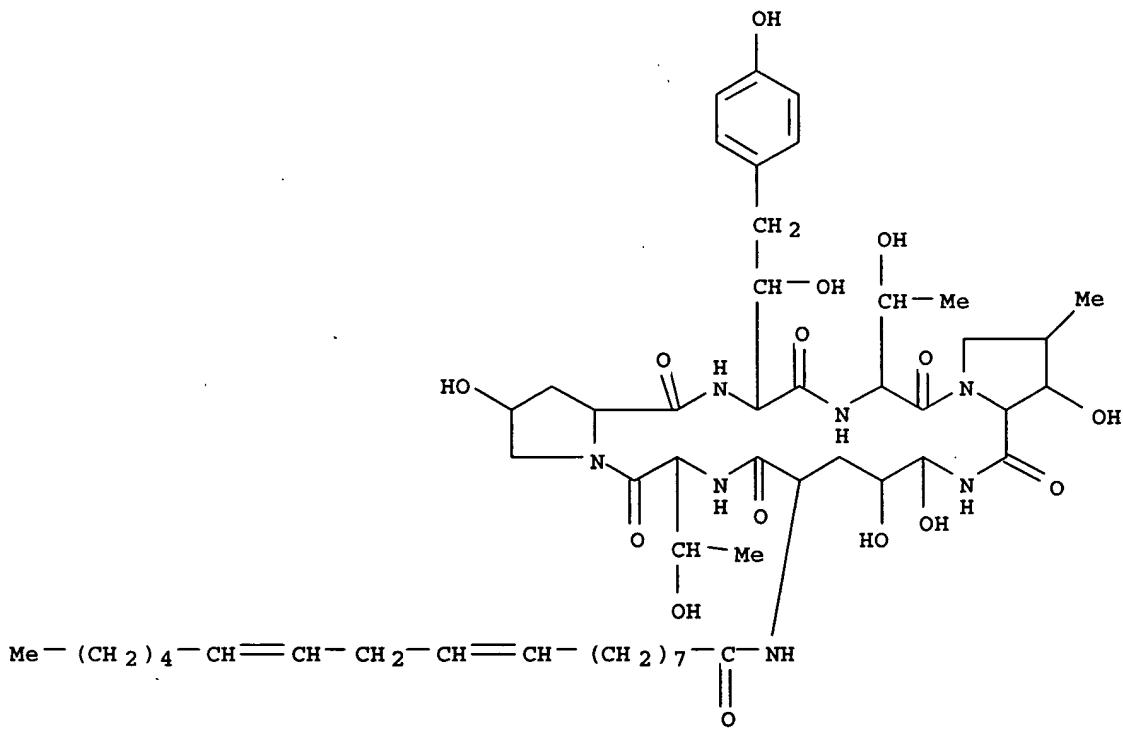
The Examiner states that amendment of claims 4, 8 and 18 introduced new matter. The Applicants strenuously object to such a characterization and assert that the amendment of these claims to include the limitation “R⁷ is —CH₃” does not add new matter. Indeed, as stated in the response to Office Action filed with the Office on October 10, 2003, support for the limitation can be found in the structure C1 at the top of page 19, where R⁷ is —CH₃. Additionally, support for the

recited limitation can also be found on page 7, lines 8-18; page 9, lines 13-18; and pages 16-17, bridging paragraph of the specification as originally filed.

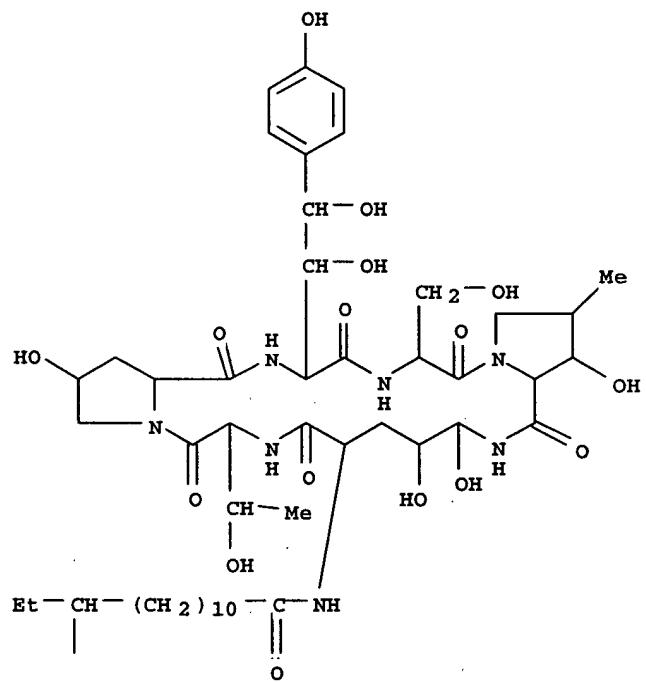
As listed above, support for the amendment of claims 4, 8, and 18 can be found particularly as exemplified in the structure C1 on page 19, and, additionally, as would be apparent to one of skill in the art, in the list of natural product starting materials on page 15. Each of Echinocandin B, Aculeacin A γ , Mulundocandin, Pneumocandin A₀, and Pneumocandin B₀ possess a —CH₃ group at the position designated R⁷ in the present application. For the Examiner's convenience, the structures of these Echinocandin cyclopeptides are reproduced below.



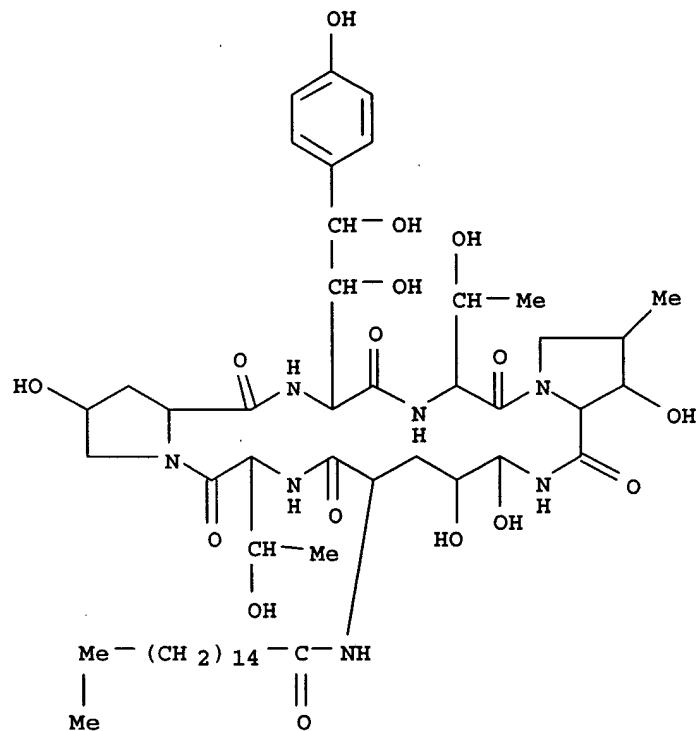
Echinocandin B



Echinocandin C



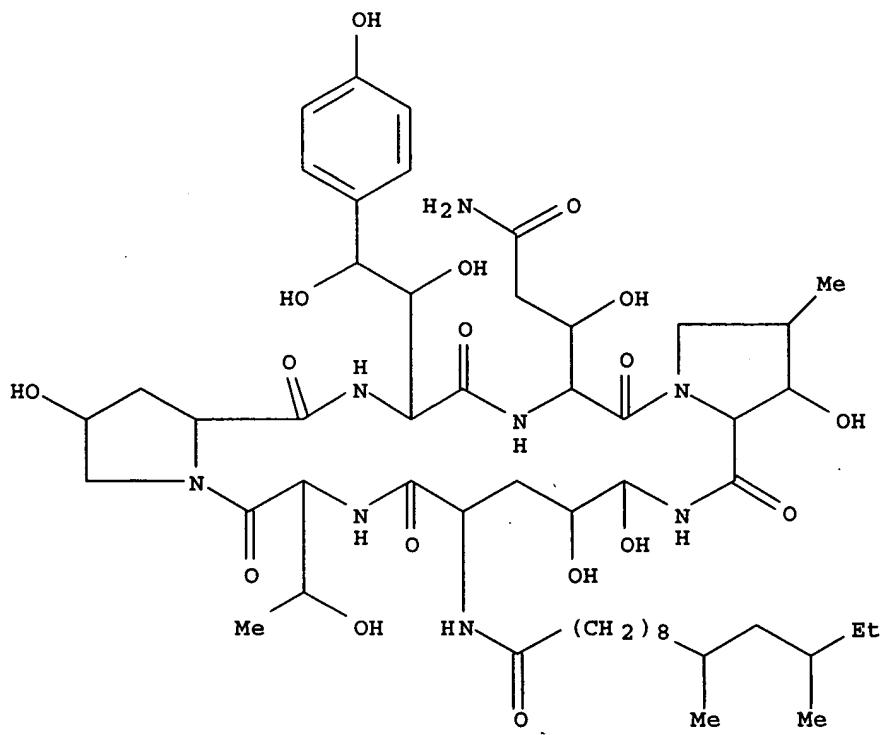
Aculeacin A

**Mulundocandin**

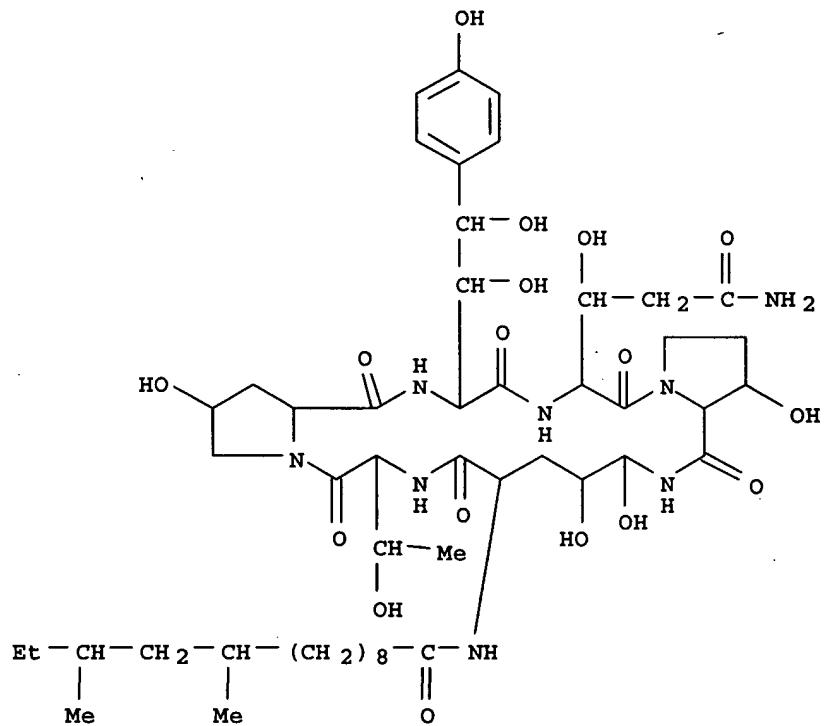
Registry Number: 82029-17-2

CA Index Name: Antibiotic S 41062F1 (9CI)

Other Names: Sporofungin



Pneumocandin A0



Pneumocandin B0

The Applicants note that there is no *in haec verba* requirement for newly added claim amendments (see MPEP § 2163 (B) reproduced below).

While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit or inherent disclosure.

And, the Applicants assert that the amendment of the claims has not added new matter and that the particular specification disclosure described above and upon which the Applicants rely for support of the amendments, is in accordance with MPEP § 2163 (B):

Further, the Applicants note that, as stated in MPEP § 2163 (I), reproduced in part below, a limitation can be described

...using such descriptive means as words, *structures*, figures, diagrams, and formulas that fully set forth the claimed invention. (Emphasis added)

And, while the Examiner states that the *literal* words of the limitation “R⁷ is —CH₃” do not appear in the specification, the Applicants assert that this limitation is amply supported not only by the disclosure of the structure C1 on page 19 (in which R⁷ is —CH₃), but also by the disclosure of the recited natural product starting materials described above and disclosed on page 15. One of skill in the art would either be familiar with the structures of the recited starting materials (in which R⁷ is —CH₃) or would be able to readily identify and review the structures to identify R⁷ in each.

In view of the above comments, the Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112 ¶1.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 342312001600. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 25, 2004

Respectfully submitted,

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